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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/653,433	09/01/2000	Zuzana Kossaczka	2026-4298US	5517

33678 7590 07/29/2003

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	25

DATE MAILED: 07/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/653,433	Kossaczka et al
Examiner	**Art Unit**
Portner	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 12, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 3-5, 12, 14, and 16-26* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 3-5, 12, 14, and 16-26* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1, 12 and 14 have been amended.

Claims 1, 3-5,12,14 and 16-26 are pending and are under consideration.

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 12, 2003 has been entered.

Rejections Withdrawn

2. Claim 14 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 39 and 44 of U.S. Patent No. (US Pat. 5,738,855), in light of the amendment of the claim to recite --comprising an N-acetyl group-- and deletion of the phrase "derived from S.typhi"

3. Claims 1, 3-5,12, and 14 under 35 U.S.C. 102(e) as being anticipated by Szu et al (October 17, 1994), in light of the amendment of the claims to no longer recite the phrase "derived from S.typhi and the insertion of the phrases "comprising an N-acetyl group" and "a carboxylic acid".

Claim Rejections - 35 U.S.C. § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1,3-5, 12, 14, 16-26 arerejected under 35 U.S.C. 103(a) as being unpatentable over Szu et al (US Pat. 5,738,855; filing date October 17, 1994).

Szu et al teach and show the formulation of a conjugate comprising Salmonella Vi antigen covalently linked through a cysteamine or cystamine linker (see col. 10, lines 30-31, teaching incorporated by reference) to Recombinant Pseudomonas (see col. 6, lines 34-35) aeruginosa exotoxinA (see Table 2, Immunogen Vi-rEPA, col. 14, line 45; col. 10, lines 30-31), wherein the native Vi antigen comprises an N-acetyl group (see col. 2, lines 59-62).

Szu et al teach a generic group of linkers which include cystamine and adipic dihydrazide (see col. 7, lines 1-3) for the conjugation of the Recombinant Pseudomonas aeruginosa exotoxinA to the polysaccharide antigen, and claims the utilization of adipic dihydrazide linker (see claim 14) in the production of the polysaccharide recombinant Pseudomonas aeruginosa exotoxinA conjugate (see col. 20, claims 10 and 44).

Additionally, Szu et al teach a method of stimulating/inducing a protective immune response through administering a dosage form (25ug, see col. 15, line9-10) of a polysaccharide-rEPA protein conjugate composition(see claims 10, 44) to a human (see claims Example 7, col. 15), as well as show the administration of Vi-rEPA to a mammal for the induction of a protective immune response (see col. 14, lines 45; col. 7, lines 17-18).

Szu et al teach Vi-rEPA compositions, the utilization of adipic dihydrazide as a linker in the formulation of a conjugate composition and methods of inducing a protective immune response through administering the Vi-rEPA composition to a mammal but differs from the instantly claimed invention by failing to show the utilization of the adipic dihydrazide to link native Vi polysaccharide antigen and rEPA in the formulation of the Vi-rEPA conjugate and the administration of the Vi-rEPA conjugate to humans.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the Vi-rEPA conjugate of Szu et al that comprised a cystamine linker with the adipic dihydrazide linker taught by Szu et al because Szu et al teaches that cystamine and adipic dihydrazide linkers are obvious variants of each other and serve to covalently link a polysaccharide to a protein carrier (see col. 7, lines 1-3), and Szu et al produced a Vi-rEPA conjugate with cystamine linker and suggested the utlization of adipic dihydrazide as a linker in polysaccharide-protein conjugates; it would be obvious to utilize the other linkers disclosed by Szu et al. in the formulation of the Vi-rEPA conjugate, specifically the adipic dihydrazide, because Szu et al teaches a limited representative number of linkers which would define means to preserve the polysaccharide immunogenicity and to obtain an enhanced immune response due to linkage to rEPA, a known adjvuant carrier protein.

Additionally, it would have been obvious to administer the Vi-rEPA adipic dihydrazide linker conjugate composition to a human in a method of inducing serum antibodies and in a method of vaccinating a human, of any age, against S.typhi infection, because Szu et al teach that Vi-rEPA served to induce an enhanced immune response over other conjugates (see Table 2, 2nd

injection), and Szu et al teach the conjugate composition to be a human vaccine (see col. 7, lines 17-29, col. 8, lines 4-8; see col. 9, lines 32-39; col. 15, lines 1-2) because the conjugate would meet the requirements set forth by the World Health Organization for a human Salmonella typhi vaccine. In the absence of a showing of unexpected results, Szu et al obviates the instantly claimed invention.

Conclusion

6. This is a non-final action.

7. Lees (US Pat. 6,309,646) is cited to show a polysaccharide-protein conjugate.

8. Kovac et al (US Pat. 5,952,454) is cited to show a method of conjugating a glycosyl donor to an amine-containing carrier or substrate material through a spacer compound.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp July 24, 2003

ANITA MINNIFIELD
PRIMARY EXAMINER
7/24/03